## REMARKS

Claims 38-44 have been canceled without prejudice and claims 24-33, 45, 46, and 50 have been amended. Support for these amendments can be found throughout the claims and specification as filed. No new matter has been added by way of amendment. Accordingly, claims 24-37 and 45-50 will be pending upon entry of this amendment.

### Information Disclosure Statement

The Examiner objected to the Information Disclosure Statement as failing to comply with the provisions of 37 CFR §1.97, 1.98 and MPEP §609 "because references A9 and A12 lack sufficient description so as to lead the reader to the cited documents". Applicants submit herewith a Supplemental Information Disclosure Statement in which Applicants provide complete descriptions for the cited information. Entry and consideration of the information cited in the enclosed Supplemental Information Disclosure Statement is respectfully requested.

### Drawings

The Examiner objected to the drawings filed July 5, 2005 as failing comply with 37 CFR 1.84(p)(5) because "they include the following reference character(s) not mentioned in the description: e.g. Fig 1A, 1B, 1C, for example." The Examiner stated that corrected drawing sheets in compliance with 37 CFR 1.121(d) or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in order to put the drawings in compliance. Applicants have amended the specification to include the reference characters for Figures 1 and 7, *e.g.* Figures 1A-1C, and Figures 7A and 7B. Applicants submit that these amendments put the drawings in compliance with 37 CFR 1.84(p)(5) and respectfully request reconsideration and withdrawal of the objection.

### Sequence Disclosures

The Examiner objected to the specification as failing to comply with the requirements of 37 CFR §1.821 through 1.825. Specifically, the Examiner objected to the specification (for example, in the Description of the Drawings) making reference to polynucleotide and polypeptide sequences without a sequence identifier of the form: SEQ ID NO:X. To address the Examiner's concerns, Applicants have amended sequence references in the specification to properly reflect the SEQ ID NO to which they are associated. For example at page 6, Applicants have amended lines 25-26 to recite "It is predicted that

amino acids 1-45 of SEQ ID NO:1 constitute the amino terminal extracellular domain..." In addition, Applicants have amended the specification to replace any sequence identifiers in the form "SEQ ID NO X" (*i.e.* those without a colon) with those of the form "SEQ ID NO:X" (*i.e.* with a colon). It is believed that the foregoing amendments overcome this objection. Thus, Applicants respectfully request reconsideration and withdrawal of the objection. However, should the Examiner be minded to maintain the objection, clarification is respectfully requested.

**Objections to the Specification**

The Examiner objected to the specification for missing ATCC numbers. Applicants have amended the specification to indicate the ATCC deposit number, PTA-1143, for the deposited cDNA clone.

The Examiner also objected to the specification for containing embedded hyperlinks and/or other forms of browser-executable code. Applicants have amended the specification to remove references to embedded hyperlinks and/or other forms of browser-executable code.

Upon entry of the foregoing amendments, Applicants submit that the objections to the specification are rendered moot. Applicants respectfully request reconsideration and withdrawal of these objections.

In addition, Applicants have amended the Related Applications section of the specification to contain specific reference to prior applications as well as indication of the relationship between the applications. The amended Related Applications section thus properly reflects the information and relationships identified in the Application Data Sheet filed February 13, 2002.

**The Rejection of Claims 24-33 and 37-50 Under 35 USC §112, Second Paragraph, Should Be Withdrawn**

Claims 24-33 and 37-50 were rejected by the Examiner under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner rejected claims 24-33 and 37-50 for the term "a complement thereof." The Examiner argued that

> "The term 'a complement of' is used ambiguously in the art and it may or may not denote a polynucleotide that is perfectly complementary to a reference polynucleotide as it may also refer broadly to any polynucleotide that may form complementary binding to the reference polynucleotide under an unspecified set of conditions. Thus, without any

> specific definition provided by the specification, the artisan could not reasonably know whether or not a given polynucleotide would be encompassed by the claims. Additionally, it is noted that the phrase "a complement thereof" places no size limitations on the claimed nucleic acid molecule."

Applicants traverse the rejection. However, in an effort to expedite prosecution, Applicants have amended the claims to remove the phrase "or a complement thereof." Applicants submit that these amendments render the rejection of claims 24-33 and 37-50 under 35 USC §112, second paragraph, moot and request reconsideration and withdrawal of the rejection.

**The Rejection of Claims 24-50 Under 35 USC §112, First Paragraph (Enablement), Should Be Withdrawn**

The Examiner rejected claims 24-50 under 35 USC §112 first paragraph, as failing to satisfy the enablement requirement, because

> "the specification, while being enabling polynucleotides encoding a polypeptide of SEQ ID NO: 1 and 4 and for naturally occurring polynucleotides that hybridize under the conditions recited at page 44 lines 19 and 20 to the polynucleotides of SEQ ID NO: 2 and 5 wherein elevated levels of said naturally occurring polynucleotides are indicative of cardiac myocyte hypertrophy, does not reasonably provide enablement for polynucleotides comprising complements of said polynucleotides, that do not hybridize as described above."

Specifically, the Examiner argues that "a complement need not be a full length complement nor a perfectly matched complement" and thus claims 24-33 and 37-50, which "require complements" of a polynucleotide of SEQ ID NO:2 or 5, "encompass any random sequence of any length as long as it has a portion of that is complementary to SEQ ID NO:2 or 5." Applicants traverse this rejection. However, in an effort to expedite prosecution, Applicants have amended claims 24-33 to remove the phrase "or a complement thereof" and canceled claims 38-44. Applicants therefore submit that the specification is fully enabling for the claimed nucleic acid molecules, vectors, host cells, etc. of claims 24-33 and dependent claims 45-50.

Claims 34-37 require polynucleotides having 95% identity with SEQ ID NO:2 or 5. The Examiner argues that specification "has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO:1 and 4," and has failed to teach how to make and use variants of the polypeptide of SEQ ID NO:1 or 4. However, Applicants note that the Examiner has stated that the specification is enabling "for naturally occurring polynucleotides that hybridize under the conditions

recited at page 44 lines 19 and 20 to the polynucleotides of SEQ ID NO: 2 and 5 wherein elevated levels of said naturally occurring polynucleotides are indicative of cardiac myocyte hypertrophy." Applicants submit that if claims directed to polynucleotide variants that hybridize to the polynucleotide sequences of the invention are found to be enabled, then surely claims directed to polynucleotide variants having a percent identity score, such as 95% identity, would also be considered enabled as the latter is more definite. Applicants respectfully submit that the currently amended claims are fully enabled within the specification as filed, as Applicants have provided teachings for every element needed for one of skill in the art to practice the claimed invention.

First, Applicants have provided the specific nucleotide and amino acid sequences of the human and murine 14273 molecules, set forth in SEQ ID NO:1, 2, 4, and 5. The specification, for example at page 15, lines 1-20, identifies specific structural regions of the 14273 GPCR, namely the seven transmembrane segments, three extracellular loop, three intracellular loops, carboxy terminal intracellular domain, and the GPCR signal transduction signature sequence with invariant arginine residue.

Second, the specification teaches one how to generate functional variants. For example, the specification at page 18 and in Table 1, teaches which substitutions may be made so that function is conserved ("conservative substitutions"). In addition, the specification at page 20, line 28 through page 22, line 6, teaches how functional variants of the 14273 molecule may be made, as well as describing useful variants and how to identify and test essential amino acid residues in the 14273 protein. Furthermore, the specification at page 5, lines 4-20, teaches that specific variants of 14273 can be associated with cardiovascular diseases (*e.g.* as in claims 34-37).

Finally, Applicants submit that one of ordinary skill in the art would be able to perform assays to determine whether or not specific sequences have the desired characteristic, *i.e.* elevated nucleic acid levels indicative of cardiac myocyte hypertrophy, and the instant specification provides examples of measuring such differences in expression levels. Applicants submit that such assays, to detect and compare the nucleic acid levels of 14273 variants in normal versus hypertrophic cardiac myocytes, would be routine for one of ordinary skill in the art. Therefore, determining whether or not a variant having 95% identity to the sequence of SEQ ID NO:2 or 5 has the desired property would not constitute undue experimentation.

Therefore, Applicants have provided all of the necessary information to enable one of skill in the art to 1) identify regions within the polynucleotide of the claimed invention which may be altered while maintaining the desired characteristics; 2) generate variants having at least 95% identity to the sequence of SEQ ID NO:2; and 3) perform assays to determine whether or not the sequences generated do in fact have the desired characteristics. Thus, contrary to the Examiner's assertions, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the currently amended claims.

In addition, the Examiner argued that the specification "does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO:1 and 4" and "has not provided guidance as to natural variants that may exist, nor how to use antibodies to specific variants that might be created." Applicants respectfully submit that natural variants, and antibodies specific to variants of SEQ ID NO:1 or 4 are not required for one of skill in the art to make and use the current invention commensurate with the scope of the claims (i.e. knowledge of natural variants or antibodies to variants are not required by the claims).

The Examiner also rejected claims 32-33 under 35 USC §112, first paragraph, as failing to comply with the enablement requirement for the following reason: "there is no indication in the specification as to public availability" of the deposited nucleic acid molecules (ATCC Accession No. PTA-1143). In response to the Examiner's concerns, Applicants have amended the specification to recite the ATCC deposit number for human 14273, as well as to include the updated address for ATCC in Manassas, VA. Applicants also submit herewith an affidavit signed by an agent of record, which states that: as required under 37 CFR 1.804(b), the plasmid containing the full length nucleotide sequence encoding human 14273 and deposited with the ATCC as Accession Number PTA-1143 on January 5, 2000, is the specific nucleic acid deposited under the conditions of the Budapest Treaty and complies with the preservation and public disclosure requirements. In addition, Applicants state that the deposit will irrevocably and without restriction or condition be released to the public upon issuance of a patent with a claim that references the deposit. Applicants respectfully request that this section 112, first paragraph rejection of the pending claims be reconsidered and withdrawn.

In view of the foregoing amendments and remarks, Applicants submit that the specification is fully enabling for one of skill in the art to practice the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24-50 under 35 USC §112, first paragraph (enablement).

## The Rejection of Claims 24-50 Under 35 USC §112, First Paragraph (Written Description), Should Be Withdrawn

Claims 24-50 were rejected by the Examiner under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner argued that

> "The specification discloses a human and murine polynucleotide of SEQ ID NO:2 and 5, respectively, yet the claims encompass polynucleotides not described in the specification, i.e. polynucleotides sequences from other species, mutated sequences, allelic variants, or sequences need that need only be 95% identical to SEQ ID NO:2 or 5. The specification contemplates these variants, see page 47-53; none of these sequences meet the written description provision of 35 USC 112, first paragraph. The skilled artisan would not be able to make useful prediction as to the nucleotide positions or identities of those sequences based on information disclosed in the specification."

The Examiner further states "the instant disclosure of a single polynucleotide from a human and a single polynucleotide from a mouse, does not adequately support the scope of the claimed genus." The Examiner concludes "only human and murine polynucleotides and polynucleotides consisting of fragments thereof, but not the full breadth of the claim meet the written description provision of 35 USC 112, first paragraph."

Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 24-33 to remove the phrase "or a complement thereof" and canceled claims 38-44, thus removing reference to fragments of the polypeptide or polynucleotide. Applicants submit that these amendments render the claims 24-33 and 38-44 fully and clearly described under 35 USC §112, first paragraph.

Claims 34-37 recite isolated nucleic acid molecules comprising nucleotide sequences with at least 95% identity to the nucleic acid sequence of SEQ ID NO:2 or SEQ ID NO:5, wherein the nucleic acid molecule further has the characteristic of elevated nucleic acid levels being indicative of cardiac myocyte hypertrophy.

"The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'" *See Union Oil Co. v. Atlantic Richfield Co.,* 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000). In particular, an adequate description can be made by disclosing identifying characteristics, such as complete or partial structure, functional characteristics, or physical and/or chemical properties. "Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph 'Written Description' Requirement," 66 Fed. Reg. 1099 (January 5, 2001). An Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*

Claims 34-37 recite isolated nucleic acid molecules comprising nucleotide sequences with at least 95% identity to the nucleic acid sequence of SEQ ID NO:2 or SEQ ID NO:5, wherein the nucleic acid molecule has the further identifying characteristic of elevated nucleic acid levels being indicative of cardiac myocyte hypertrophy. The recitation of at least 95% sequence identity is a *very predictable*

*structure* of the sequences encompassed by the claimed invention. The Examiner is reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces, 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a person of ordinary skill to envision the claimed invention, *i.e.*, nucleotide sequences with at least 95% identity to the nucleic acid sequence of SEQ ID NO:2 or SEQ ID NO:5, and as described above, it would be routine for one of ordinary skill in the art to determine if such a variant would also have the characteristic of elevated nucleic acid levels being indicative of cardiac myocyte hypertrophy.

Example 14 of the Revised Interim Written Description Guidelines is directed to a generic claim: a protein having at least 95% sequence identity to the sequence of SEQ ID NO:3, wherein the sequence catalyzes the reaction A to B. The Training Materials concludes that the generic claim of Example 14 is sufficiently described under 35 U.S.C. §112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus" and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A to B. The Guidelines conclude that one of skill in the art would recognize the necessary attributes possessed by the members of the genus.

Following the analysis of Example 14, Applicants submit that claims 34-37, and dependent claims 45-50 therefrom, satisfy the written description requirements of 35 U.S.C. §112, first paragraph. Specifically, the claims of the present invention encompass nucleic acid molecules with sequences having at least 95% sequence identity to the sequence of SEQ ID NO:2 or SEQ ID NO:5, wherein elevated nucleic acid levels of the polynucleotide are indicative of cardiac myocyte hypertrophy. As in Example 14, the specification discloses the nucleotide sequence of SEQ ID NO:2 and 5, and the claims recite the specific limitation of the compound wherein elevated nucleic acid levels of the polynucleotide are indicative of cardiac myocyte hypertrophy.

In summary, the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus in the currently amended claims would be clearly recognized by one of skill in the art and consequently, the Applicant has disclosed the necessary common attributes or features of the elements possessed by the members of the genus of claims 34-37. Accordingly, in view of these remarks and those above for claims 24-33 and 38-50, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. § 112, first paragraph rejection over claims 24-50.

**The Rejection of Claims 24- 33, 38-41, and 50 Under 35 USC §102(e) Should Be Withdrawn**

Claims 24, 26, 28, 30, 32, 33, 38, and 50 were rejected by the Examiner under 35 USC §102(e) as being anticipated by U.S. Patent Serial No. 5,789,223. Claims 25, 27, 29, 31, and 39-41 were rejected by the Examiner under 35 USC §102(e) as being anticipated by GenBank Accession number AA030752.

Specifically, the Examiner argues that U.S. Patent 5,789,223 discloses a polynucleotide that is 100% identical to the instant SEQ ID NO: 2 over a region of 45 base pairs, and that positions 4083-4039 of the sequence disclosed in 5,789,223 would be considered an isolated polynucleotide comprising a complement of SEQ ID NO: 2, and presumably the polynucleotide deposited as PTA-1143 as well. In an effort to expedite prosecution, Applicants have amended the claims to remove the phrase, "or a complement thereof." In addition, Applicants have canceled claims 38-44, drawn to polynucleotide and/or polypeptide fragments. Applicants therefore submit that the sequences disclosed in U.S. Patent Serial No. 5,789,223 and by GenBank Accession number AA030752 no longer fall within the scope the claimed invention, rendering the rejection moot. Applicants respectfully request reconsideration and withdrawal of this rejection.

## CONCLUSIONS

In view of the amendments and remarks made herein, Applicants respectfully submit that the objections and rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

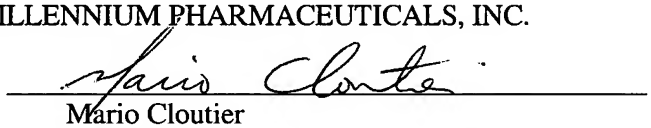
This paper is being filed timely as Applicants believe no extension of time is required. In the event any extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

May 4, 2005

MILLENNIUM PHARMACEUTICALS, INC.

By 

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